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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,399	02/10/2004	Henry Li	016556-003610US	2418

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EXAMINER
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SHIBUYA, MARK LANCE

ART UNIT	PAPER NUMBER
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1639

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/776,399

Applicant(s)

LI ET AL.

Examiner

Mark L. Shibuya, Ph.D.,

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 9-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-87 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/27/04 and 7/17/05</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

1. Claims 1-12 are pending. Claims 9-12 are withdrawn from consideration.

Claims 1-8 are examined.

***Election/Restrictions***

2. Applicant's election of Group I, claims 2-8 in the reply filed on 9/20/2006, is acknowledged. In electing so-called Group I, applicant states that applicant selects, as a species, nuclear hormone receptors.

Applicant's election of the species:

(A/T/G) (C/T) (A/G/T/C) TG(T/C) (A/G) (A/G) (A/C/G/T)  
T/S/A C D/E/G/N

(A/G) (C/G) (A/C/G/T) TG(T/C) (A/T) (A/C/G) (A/C/G)  
G/S/A C K/S

(A/G) (C/G/T) (A/C/G/T)  
G/S/N/A

in the reply filed on 9/20/2006, is acknowledged. Apparently, this is disclosed as a 21 nucleotide consensus sequence/signature motif, in the specification, at pp. 18-22, which is a "zinc finger domain present in all 45 known members of the nuclear hormone receptor family." Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

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3. The examiner respectfully notes that the requirement for election/restriction, mailed 8/23/2006, stated that claim 1 was a linking claim that links numerous inventions of families of proteins, including the invention of nuclear hormone receptors, as selected. This requirement for linking claim restriction is maintained. Therefore, the election of a species that is nuclear hormone receptor, is taken as an election of invention. The examiner respectfully maintains that the various families of protein do not have a common peptide structure responsible for a common property with one another, such that the various families of protein have unity of invention.

4. Claims 9-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/20/2006.

***Priority***

5. This application, filed 2/10/2004, claims benefit of provisional No. 60/446,714, filed 2/11/2003.

***Information Disclosure Statement***

6. The information disclosure statements (IDS) submitted on 7/27/2004 and 7/17/2005, were filed before the mailing date of the Requirement for Restriction/Election on 8/23/2006. The submission is in compliance with the

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provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. Citation AI of the IDS, filed 7/27/2004, has been corrected by the examiner to show the year of publication.

### ***Specification***

7. The use of the trademark "Inverse Genomics" on p. 4 of the instant specification, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### ***Claim Rejections - 35 USC § 112, First Paragraph***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

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time the application was filed, had possession of the claimed invention. This rejection is for lack of written description.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The specification as filed does not disclose a representative number of species of consensus sequences adequate to disclose the genus of all families of proteins. Wolf et al., J. Mol. Biol. (2000), Vol. 299, pp. 897-905, throughout the publication, and in the abstract, estimate the number of protein families with significant sequence conversation to be between 4000 and 7000, with structures available for about 20% of these. Wolf et al., at pp. 897-898, bridging paragraph, states that different groups have estimated from 1000 to 30,000 for the number of families.

Opalinska et al., Nature Reviews, Drug Discovery, (July 2002), Vol. 1, pp. 503-514, throughout the publication, teach the unpredictability of technologies, such as siRNA inhibition of expression, in that the ability of nucleic acid molecules to modify gene expression *in vivo* is quite variable and therefore wanting in terms of reliability. For example, Opalinska et al., at p. 511, state: "In mRNA, sequence accessibility is dictated by internal base pairing and the

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proteins that associate with the RNA in a living cells." Opalinska et al., at pp. 511-512, bridging paragraph teach that siRNA delivery into cells, *in vivo*, and effective inactivation of targets is unpredictable.

One of skill in the art cannot envision the detailed consensus nucleotide sequences encoding all known motifs of families of proteins, which would be targeted by siRNA libraries, and that would inhibit all members of all known families. The specification does not provide the peptide sequence of the motifs of all protein families, or the consensus nucleotide sequences that encode the motifs. The art teaches that there are thousands of families of proteins. The specification does not provide any sequence or chemical structure of Alpha 2-HS glycoprotein that correlates with induction of apoptosis. The specification provides only a few of these families, and provides no working embodiments of methods of making such siRNA libraries that are capable of inhibiting post-transcriptional silencing. The specification does not point to where in the art such information exists. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

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10. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating an siRNA expression library for selective post-transcriptional silencing of genes encoding a family of proteins, does not reasonably provide enablement for generating libraries for selective post-transcriptional silencing of genes in the whole animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

However, there is insufficient guidance as to how to make and use any . There are many factors be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether undue experiment is necessitated.

These factors can include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the relative skill of those in the art;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1 and 2) The breadth of the claims and the nature of the invention:

The claims are drawn to a method for generating an siRNA expression library for selective post-transcriptional silencing of genes encoding a family of proteins, the method comprising: i. identifying a consensus sequence for the family of



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proteins; and, ii. generating an siRNA expression library whose members encode siRNA molecules that target at least all mRNA encoding all known members of the family of proteins; and variations thereof. Thus the claims are very broad in scope of encompassed subject matter, being drawn to any signature motif of any family of protein.

(3 and 5) The state of the prior art and the level of predictability in the art:

Opalinska et al., Nature Reviews, Drug Discovery, (July 2002), Vol. 1, pp. 503-514, throughout the publication, teach the unpredictability of technologies, such as siRNA inhibition of expression, in that the ability of nucleic acid molecules to modify gene expression *in vivo* is quite variable and therefore wanting in terms of reliability. For example, Opalinska et al., at p. 511, state: "In mRNA, sequence accessibility is dictated by internal base pairing and the proteins that associate with the RNA in a living cells." Opalinska et al., at pp. 511-512, bridging paragraph teach that siRNA delivery into cells, *in vivo*, and effective inactivation of targets is unpredictable.

Wolf et al., J. Mol. Biol. (2000), Vol. 299, pp. 897-905, throughout the publication, and in the abstract, estimate the number of protein families with significant sequence conversation to be between 4000 and 7000, with structures available for about 20% of these. Wolf et al., at pp. 897-898, bridging paragraph, states that different groups have estimated from 1000 to 30,000 for the number of families. Thus Wolf et al., teach unpredictability in determining the true scope of families of proteins.

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(4) The level of one or ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6-7) The amount of direction provided by the inventor and the existence of working examples: The specification discloses a few species of consensus sequences for a few families of proteins. The specification does not provide an embodiment, working or otherwise, of any library of siRNA. The specification does not provide an embodiment, working or otherwise, of any siRNA molecules that target, *in vivo*, at least all mRNA encoding all known members of a family of proteins and the post-transcriptional silencing of that family of proteins.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The claims contain only broad recitations of post-transcriptional silencing of families of proteins, *in vivo*. However, the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in carrying out the full scope of the claimed methods. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 and n.23, 20 USPQ2d 1438, 1455 and n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant

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disclosure, undue experimentation would be required of one of skill in the art to practice the full scope of the claimed invention.

***Claim Rejections - 35 USC § 112, Second Paragraph***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7 and 8, and their dependent claims, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The claims do not recite steps that provide a nexus between the step of identifying a consensus sequence for a family of protein and the step of generating an siRNA expression library. There is no step providing a nexus or structural relationship between molecules that target mRNA of a family of proteins, and the consensus sequence for the family of proteins.

Applicant's usage of the language of "all known members" of a family of proteins, (as in claim 1) appears to read upon a mental step. It unclear as to whom the family of proteins are "known". Also, it is unclear as to whether the language refers to a mental step or attempts to refer to a structural limitation of the claimed product. It is not disputed that applicant may be their own

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lexicographer. The examiner does not argue that the term is repugnant to the usual usage in the art. Rather, it is that claim 1 does not reasonably apprise of one skill in the art as to the metes and bounds of the claimed invention.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-3, 6 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Agami et al., US 2003/0144232 A1.

The claims are drawn to a method for generating an siRNA expression library for selective post-transcriptional silencing of genes encoding a family of proteins, the method comprising: i. identifying a consensus sequence for the family of proteins; and, ii. generating an siRNA expression library whose members encode siRNA molecules that target at least all mRNA encoding all known members of the family of proteins; and variations thereof .

Agami et al., US 2003/0144232 A1, throughout the publication and at para [0195]-[0200], teach methods for generating an siRNA expression library for selective post-transcriptional silencing of genes (Agami et al., at para [0015]-[0017]), including a single siRNA able to target several genes, typically specific for a sequence present in two or more genes such as an evolutionary conserved sequence in a gene family thereby inhibiting a particular gene class, (Agami et al., at para [0195]-[0200]), which reads on and describes targeting genes encoding a family of proteins, the method comprising: i. identifying a consensus sequence for the family of proteins; and, ii. generating an siRNA expression library whose members encode siRNA molecules that target at least all mRNA encoding all known members of the family of proteins.

Agami et al., US 2003/0144232 A1, at para [0094], [0198], teach the region of sequence identity to the target gene is from 18-30 nucleotides in length, reading on a consensus sequence between 18 to 24 nucleotides, as in claims 2 and 3.

Agami et al., US 2003/0144232 A1, throughout the publication and at para [0118], teach targeting a gene that encodes, for example, a membrane channel, reading on an ion channel, as in claim 6.

***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Agami et al., US 2003/0144232 A1**, and in view of **Finney et al., US 2003/0143597 A1**.

The claims are drawn to a method for generating an siRNA expression library for selective post-transcriptional silencing of genes encoding a family of proteins; and wherein the library numbers between 20,000 and 100,000 members.

**Agami et al., US 2003/0144232 A1**, is relied upon as above.

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Agami et al., does not disclose a method for generating an siRNA expression library, wherein the library comprises between 20,000 and 100,000 unique members.

**Finney et al., US 2003/0143597 A1**, throughout the publication teach nucleic acid technologies, including siRNA, for the inhibition of gene expression, and state:

[0011] Other technologies are used to gain direct information about effects of gene products on phenotypes associated with human tissues, diseases and disorders. Such information may be sought by: (i) over-expressing a gene product; (ii) disrupting a gene's transcript, such as by disrupting a gene's mRNA transcript; (iii) disrupting the function of a polypeptide encoded by a gene; or (iv) disrupting the gene itself. Over-expression of a gene product and the use of antisense RNAs, ribozyme and double-stranded RNA interference (dsRNAi) techniques are also valuable in discovering inhibitors of gene products and for generating gene knockouts.

...

[0013] Antisense RNA, ribozyme, and dsRNAi technologies typically target RNA transcripts of genes, usually mRNA. Antisense RNA technology involves expressing in, or introducing into a cell, an RNA molecule (or RNA derivative) that is complementary to, or antisense to, sequences found in a particular mRNA into a cell. By associating with the mRNA, the antisense RNA can inhibit translation of the encoded gene product. Similarly, a ribozyme is an RNA that has both a catalytic domain and a sequence that is complementary to a particular mRNA. The ribozyme functions by associating with the mRNA (through the complementary domain of the ribozyme) and then cleaving (degrading) the message using the catalytic domain. Limited examples of use of double-stranded RNA (dsRNA) molecules, in a technique known as "RNA interference" are currently known for mammalian cells. It is believed that small (15-23 nucleotides, preferably 21-23 nucleotides) dsRNA molecules introduced into mammalian cells can associate with mRNA and induce degradation of that specific mRNA transcript (see WO 01/75164).

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Finney et al., at para [0013]. Finney et al., at para [0322], [0342], teach siRNA libraries comprising modified or disrupted genes, reading on unique members, numbering at least 20,000, as in claims 4 and 5.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used a method for generating an siRNA expression library, wherein the library comprises between 20,000 and 100,000 unique members; and wherein the library encoded a family of proteins.

One of ordinary skill in the art would have been motivated to make and use siRNA libraries because Finney et al., at para [0360]-[0384], and e.g., at [0362], teach libraries as well suited for identifying the molecular basis for identifying the molecular basis for genetically determined advantages, such as prolonged life-span; and because Agami et al., suggest the inhibition of a class of genes in a cell.

One of ordinary skill in the art would have had a reasonable expectation of success in making siRNA libraries comprising 20,000 unique members, because Finney et al., teach that such libraries were used in the art.

17. Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Agami et al., US 2003/0144232 A1**, and in view of **Finney et al., US 2003/0143597 A1**, as applied to claims 1-7 above, and further in view of **Chinn et al., US 2003/0215829 A1**.



The claims are drawn to a method for generating an siRNA expression library for selective post-transcriptional silencing of genes encoding a family of proteins; comprising identifying a consensus sequence for a family of nuclear hormone receptor proteins, making a siRNA library for silencing expression of nuclear hormone receptor proteins; and wherein two or more signature motif variant are identified.

**Agami et al., US 2003/0144232 A1, and Finney et al., US 2003/0143597 A1,** are relied upon, as above.

Agami et al., US 2003/0144232 A1, and Finney et al., US 2003/0143597 A1, taken together, do not teach or suggest a family of nuclear hormone receptor proteins, whose expression is targeted by siRNA, and the methods of making siRNA expression libraries, thereof. Agami et al., US 2003/0144232 A1, and Finney et al., US 2003/0143597 A1, taken together, do not teach or suggest identifying a consensus sequence comprising identifying two or more variants of a signature motif for a family of protein.

**Chinn et al., US 2003/0215829 A1,** throughout the publication, and abstract, teach antagonists of the superfamily of human nuclear hormone receptors. Chinn et al., at para [0222], teach screening of combinatorial libraries of oligonucleotides for antisense activity against nuclear hormone receptors expression. Chinn et al., at para [0279], teach analysis of the consensus primary structures of gene families. Chin et al., at e.g., para [0045], [0141], Table 3, teach identifying predicted motifs and domains of polypeptide families of nuclear hormone receptors, reading on identifying two or more variants of a signature

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motif for a family of protein, as in claims 7 and 8. Chinn et al., at para [0238], teach probes to motifs as conserved, less specific regions, for identifying naturally occurring sequences encoding nuclear hormone receptors (NHREC), allelic variant, and related sequences.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used methods of making siRNA expression libraries, comprising identifying a consensus sequence for a family of nuclear hormone receptor proteins, making an siRNA, for silencing expression of nuclear hormone receptor proteins; and wherein two or more signature motif variant are identified.

One of ordinary skill in the art would have been motivated to make and use methods of making siRNA expression libraries, comprising identifying a consensus sequence for a family of nuclear hormone receptor proteins; because Agami et al. teach siRNA libraries directed against the consensus sequences of protein families to inhibit classes of proteins, Finney et al., suggest nucleic acids, such as antisense and siRNA for inhibiting gene expression for the beneficial control of cell characteristics, and Chinn et al., teach the antisense inhibition of the expression of superfamily of nuclear hormone receptor proteins. Chinn et al., teach two or more variants of a signature motif for identifying variants and related sequences of said nuclear hormone receptor protein superfamily.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using siRNA libraries to target the expression of the superfamily of nuclear hormone receptor proteins, because Agami et al., and

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Chinn et al., teach consensus sequences for nucleic acids encoding protein families generally, and nuclear hormone receptor protein, specifically and respectively; and variants of signature motifs. Furthermore, Agami et al. and Finney et al., teach the siRNA for inhibiting gene expression.

### ***Conclusion***

18. Claims 1-8 are rejected.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya, Ph.D., whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mark L. Shibuya, Ph.D.,  
Primary Examiner  
Art Unit 1639